EXHIBIT 3

DECLARATION OF DR. KANWALJEET S. ANAND

I am Dr. Kanwaljeet S. Anand, M.B.B.S., D.Phil., FAAP, FCCM, FRCPCH who files this declaration under penalty of perjury. I am a pediatrician specialized in the care of critically ill newborns and children. I serve as a fully tenured Professor of Pediatrics, Anesthesiology, Perioperative & Pain Medicine at Stanford University School of Medicine, and as Director of the Pain/Stress Neurobiology Laboratory at Children's Hospital Research Institute. For more than 30 years, I have conducted intensive research and study on the development of pain/stress in human newborns, their development during early childhood, and long-term outcomes. I have authored 311 scientific publications (125 in the last 10 years), edited 9 books, and received numerous professional awards. My true and correct Curriculum Vitae is attached. I am personally familiar with Opioid Use Disorder in adult females and Neonatal Abstinence Syndrome and have reviewed the materials referenced below.

The President of the United States had declared a national medical emergency caused by the Opioid Crisis in America[1]. The immediate effects of the Opioid Crisis, however, may be strikingly less consequential when compared to its effects on the individuals who were exposed to opioid drugs prenatally, many of whom were diagnosed with NAS. These children, through no fault of theirs, have been condemned to suffer from the short-term and long-term effects of opioid exposure from birth throughout their childhood, adolescence and into their adult lives. Though the current Opioid Crisis looms large on the thinking of social, medical, or government establishments, but its long-term impact is inestimable because of the pervasive and persistent effects of prenatal opioids on all aspects of an individual's development. Their cumulative burden of suffering, and the total impact of their exposures on all facets of our society is so huge and unparalleled in human history that this is truly the real emergency. Unless they are monitored/supported/treated NOW, the problems of these children will become intractable and unmanageable as they grow into adulthood, wiping away generations of human endeavor because of our short-sightedness. I offer the following statements for the Court's consideration:

Definitions

- Opioid Use Disorder (OUD) is defined in the DSM-5 as a problematic pattern of opioid use leading to clinically significant impairment or distress. OUD was previously classified as Opioid Abuse or Opioid Dependence in DSM-IV.
- OUD has also been referred to as "opioid addiction" in previous publications. Addiction is defined as a chronic, relapsing syndrome of psychological dependence and craving of a drug for its psychedelic, sedative, or euphoric effects; characterized by compulsion, loss of control, and continued use of a substance despite knowledge of its harmful effects[2].
- Infants and children are not "users" as defined under the DSM-5 criteria and are excluded from the class of persons suffering from OUD. Regardless, the birth mothers of children diagnosed with neonatal abstinence syndrome (NAS) would be included within the definition of OUD.
- Neonatal abstinence syndrome (NAS) or neonatal opioid withdrawal syndrome (NOWS) are terms used to denote a group of problems that occur in the children who were exposed to opioid or opiate drugs in the mother's womb. NAS is diagnosed clinically based on the clinical signs occurring in the 1 week after birth, characterized by neurologic hyperexcitability, gastrointestinal dysfunction, and autonomic instability. Most common neurologic signs include anxiety, agitation,

grimacing, insomnia, increased muscle tone/reflexes, exaggerated startle reflexes, high-pitched crying, tremors and abnormal movements, seizures; gastrointestinal symptoms include vomiting, diarrhea, poor sucking, dehydration; autonomic signs include elevated heart rate, respiratory rate, and blood pressure, fever, sweating, mottled skin, yawning, skin excoriation, cold extremities[2-5].

Notes: 1. Most clinicians diagnose NAS in children with modified Finnegan score of 8 or greater from two (2) consecutive assessments performed by a qualified healthcare practitioner with a minimum interval of 4 hours between the two consecutive NAS assessments[6-9]. Although the Finnegan NAS was criticized in various publications and alternatives were suggested, however, it is still the most widely used method for making a clinical diagnosis of NAS[10,11]. Simplified versions of the Finnegan NAS scale were developed and cross-validated against the original Finnegan score but did not show any significant improvement in psychometric properties[12-14]. Other methods for making the NAS diagnosis include the Rivers opiate withdrawal tool[15], the Lipsitz narcotic withdrawal score (cut-off score of 4 or more indicates NAS)[14], the neonatal narcotic withdrawal index (cut-off score of 5 or more indicates NAS)[16], and other less commonly used methods. Two recent studies have substantiated the validity of a clinical diagnosis for NAS coded within the patient's medical record at the time of hospital discharge[17,18]. A quality improvement (QI) initiative showed increases in the accuracy and consistency of Finnegan NAS scoring by nurses, but the effects of this training were short-lasting[19].

2. Although all children born to birth mothers suffering from OUD in pregnancy may or may not show signs/symptoms of NAS or NOWS, their brain development has been altered by repeated exposures to opioid drugs in the prenatal period. NAS signs/symptoms are the clinical manifestations resulting from sudden withdrawal of the prenatal opioid exposure, whereas the structural and functional alterations in their brain cells, connections, and architecture, as well as the brain damage from opioid-induced apoptosis (programmed cell death) occurs long before a child is born. These changes in brain development are permanent and will affect these children throughout their entire lifespan (see below). Therefore, we need to establish a class of individuals who were exposed to opioid drugs prenatally, particularly those who were diagnosed with NAS/NOWS after birth.

3. For the purposes of monitoring and surveillance, therefore, the following objective criteria will identify children with NAS and at risk for long-term neurodevelopmental consequences of prenatal opioid exposures:

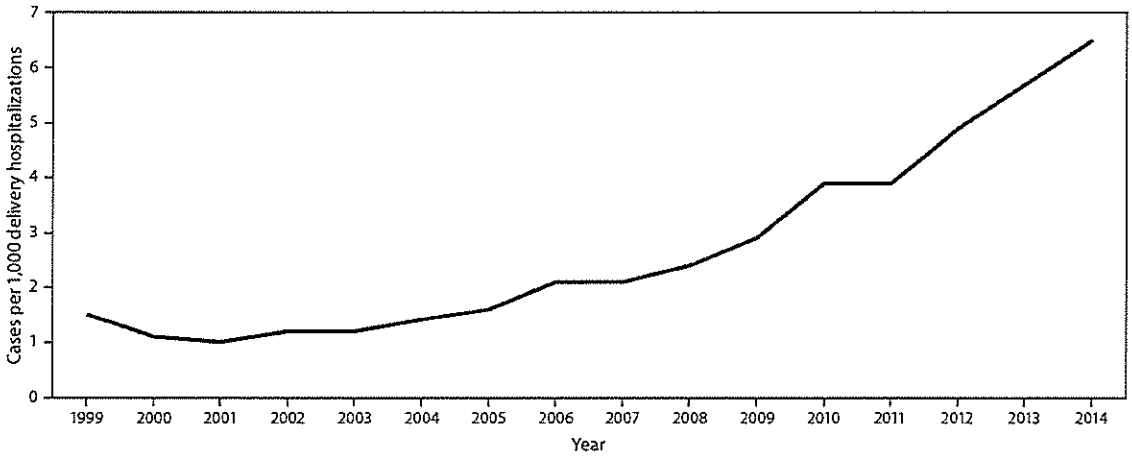
a) Diagnosis of NAS or NOWS documented in the child's medical record, for example, using the diagnostic codes of: P96.1/P04.49 (ICD-10 CM), 779.5/760.72 (ICD-9 CM)[18]; and/or
b) Monitoring of NAS/NOWS score(s) after birth, meeting the diagnostic criteria as defined above; and/or
c) Postnatal weaning of opioid drugs (morphine, methadone, buprenorphine, or other opioids); and/or
d) Children who are already listed in a national registry or other registries established for NAS[20]; and/or
e) Toxicology screen of (a) maternal blood, urine, or hair analysis, (b) umbilical cord blood, (c) baby's meconeum testing positive for opioids (excluding mothers who were prescribed opioids after the onset of, or for the purpose of treating labor pains, or for treating procedural pain).

The numbers of babies exposed to prenatal opioids annually

1) Based on trend analyses for birth mothers suffering from OUD in pregnancy, approximately 36,000 babies are likely to be born with prenatal opioid exposures in 2018[21] (projected using the CDC birth rate data)[22-24]. CDC data show that the documented rate for birth mother OUD was 6.5 per 1,000 delivery hospitalizations in 2014 (MMWR, August 2018[21]). This is a conservative estimate, since it does not include babies delivered at home, at maternity clinics, or birthing centers. Epidemiological studies show that rates of birth mother OUD may be higher among women who use non-hospital birthing centers or prefer delivering their baby at home[21,25-27].

2) Using data from 1999 to 2014[21], the National Average Annual increase in opioid exposed birth rates for mothers suffering from OUD was 0.39 per 1,000 delivery hospitalizations per year. This estimate averages the increases in birth mother OUD rates over 16 years of collected data, although the rate of increase was much greater in the last 5 years of data collection (Figure 1).

FIGURE 1. National prevalence of opioid use disorder per 1,000 delivery hospitalizations* — National Inpatient Sample (NIS),† Healthcare Cost and Utilization Project (HCUP), United States, 1999–2014



Even using this conservative yearly rate increase (3.9%) will give us prenatal opioid exposure rates increasing up to 8.45 per 1,000 delivery hospitalizations in 2019. However, if we project the prenatal opioid exposure rate increases from the past 5 years, National Average increases show an increased rate of 7.2% or 0.72 per 1,000 delivery hospitalizations per year. This will give us prenatal opioid exposure rates increasing to 10.1 per 1,000 delivery hospitalizations in 2019. These data are listed in **Table 1** on the next page. Table 1 also includes the "corrected" prenatal opioid exposure rates after adjusting for: (1) women undergoing detox before the baby's birth, whose babies may not show signs of NAS; and (2) those women who do not deliver in a hospital (previous studies have reported higher OUD rates among these women).

Annual growth rate of individuals at risk for NAS

3) More than half (60-75%) of the individuals born to birth mothers with OUD in pregnancy are expected to be diagnosed with NAS as defined above[21,28-36]. Those diagnosed with NAS are more likely than non-NAS individuals to have more significant exposures to prenatal opioids and to have developed subcellular and other physiological changes as a result of such exposures. CDC states that individuals at risk for NAS are **"clearly underestimated and under-reported"** but

the data available from 36 states in 2015 showed approximate increases of 7.2% occurring in each year between 2011 and 2015[21,26,27,37,38].

Table 1: Numbers of Individuals at risk for NAS: Trend analyses from 2014 to 2019

	National Average Increase 0.39/year (**1999-2014** data)			National Average Increase 0.72/year (**2011-2014** data)			Estimates including babies who detox *in utero* and those born in non-hospital settings		
	OUD rate/1000 hospital deliveries	Number of live-births: CDC data	Newborns with prenatal opioid exposures	OUD rate/1000 hospital deliveries	Number of live-births: CDC data	Newborns with prenatal opioid exposures	Corrected OUD rates/1000 live births	Number of live-births: CDC data	Newborns with prenatal opioid exposures
2014	6.5	3,988,076	25,922	6.5	3,988,076	25,922	7.5	3,988,076	29,911
2015	6.89	3,978,497	27,412	7.22	3,978,497	28,725	8.5	3,978,497	33,817
2016	7.28	3,945,875	28,726	7.94	3,945,875	31,330	9.4	3,945,875	37,091
2017	7.67	3,853,472	29,556	8.66	3,853,472	33,371	10.3	3,853,472	39,691
2018*	8.06	3,776,403	30,438	9.38	3,776,403	35,423	11.1	3,776,403	41,918
2019*	8.45	3,738,639	31,591	10.1	3,738,639	37,760	11.9	3,738,639	44,490

*2018 Number of Live-births estimated with a 2% decrease in births from 2017; *2019 Number of Live-births estimated with a 1% decrease in births from 2018

Constellation of clinical conditions associated with NAS

4) Opioids are proven hazardous substances for prenatal human development. Thus, NAS is associated with premature birth, low birth weight, intrauterine growth retardation (IUGR), perinatal or neonatal mortality, increased birth defects, delayed cognitive development, long-term behavioral problems, ADHD, auditory deficits, speech delay, swallowing difficulty, gastro-esophageal reflux disease (GERD), digestive or gastrointestinal motility disorders, delayed feeding, failure to thrive, congenital neurological defects, and congenital heart defects[39-45].

Time periods of interventions to achieve the best outcomes

5) For most of the conditions listed above, the best possible outcomes can only be achieved with proper management of NAS before hospital discharge, coupled with increased monitoring and surveillance, as well as active multi-disciplinary interventions that are initiated just after birth and continued for the child's entire childhood and adolescence (up to 18 years of age)[30,39,46-56].

Evidence suggesting that prenatal opioid exposure damages DNA

6) Huge amounts of published data substantiate the findings that prenatal opioid exposures alter genetic regulation and DNA structure, although many of these studies were performed in animal models[57]. Almost 40 years ago, however, leading researchers discovered that prenatal opioid

exposure damages human DNA and/or prevents DNA repair occurring from other causes of DNA damage (e.g. UV light)[58]. Since then, accumulating data have shown the progressive and persistent effects of repetitive prenatal opioid exposure on DNA fragmentation occurring in the developing human brain and in peripheral blood cells[58-71]. More recently, several studies also documented the epigenetic effects of opioid addiction, capable of intergenerational and transgenerational transmission to the offspring of opioid addicts[72-80]. Although pregnant women were excluded from some of these studies, the underlying mechanisms are the same and will have extensive effects on the massive amounts of DNA synthesis occurring during prenatal human development[66,81].

Consequent to the opioid effects on human DNA cited above, a large number of studies have found a higher incidence of birth defects in the babies exposed to maternal opioids *in utero*[45]. Seventeen (17) studies found opioid exposure linked with facial/oral defects (e.g., cleft lip, cleft palate, or others), heart defects (e.g., ventricular septal defects, atrial septal defects, hypoplastic left heart syndrome, pulmonary valve stenosis, conoventricular septal defects), limb deformities (e.g., clubfoot), visceral organ defects (e.g., gastroschisis), or neural tube defects (e.g., spina bifida)[40,41,43-45]. Most of these conditions require multiple surgical operations and long-term medical care to support the optimal development of these severely affected children[43,82].

Long-term cognitive and behavioral outcomes of individuals diagnosed with NAS

7) Brain Development: Opioids have drastic and sustained effects on brain development in the fetal and postnatal periods, affecting the brain's size, architecture, networks and connections between brain cells, neurochemical and other functions of each cell, as well as the brain DNA's structure, its expression and regulation. Thus, prenatal opioid exposures have robust and long-term effects on the cognitive and behavioral outcomes of the individuals diagnosed with NAS[82]. Opioids affect brain development by disrupting oligodendrocyte development, altering the temporal sequencing and quality of nerve fiber myelination[83], decreasing the growth of nerve cell dendrites[84,85] and their branching pattern complexity of pyramidal neurons in the cerebral cortex[40], and by suppressing cell proliferation and neuronal migration to the cortical plate[86]. These effects may reduce regional brain volumes in the basal ganglia[87] and other brain areas[87-90], with lower developmental potential.

8) Brain Growth: A large number of studies have reported lower birth weights and smaller head circumferences in opioid-exposed babies with relatively increased risks in those exposed [20,36,87,91-99]. A controlled comparison showed that reduced fetal head and body growth in infants of opioid-dependent mothers were not explained by gestational age, cigarette smoking, area deprivation, infant gender, maternal age or parity[100]. Given the limited maternal/environmental effects on head circumference, it is likely that the robust effects of opioid exposure on head circumference occur by reducing brain growth[82,101]. This was confirmed in a pilot study of 16 infants, where volumetric MRI scans showed smaller whole brain volumes and basal ganglia volumes compared to age-matched population means[87]. In another follow-up MRI study that included 38 youths in the opioid-exposed group and 44 youths in the non-exposed group (aged 17 to 22 years), the drug-exposed group displayed smaller brain volumes, smaller surface areas of the cerebral cortex, and thinner cortical mantles than unexposed youth[88].

9) Functional Effects: The consequences of this impaired brain growth are also pervasive, with altered dyadic interactions between mothers and infants[102], impaired early development in all domains of the Griffith's Mental Development Scales[103], impaired visual acuity and visuomotor

functions (eye-hand coordination)[101,103,104], impaired language-related cognitive skills and executive functions[105,106], with inattention, hyperactivity, impulsivity, aggression, ADHD, other social and behavioral problems persisting into adolescence and even adulthood in those born to opioid-dependent mothers during pregnancy[88,91,107-109]. Baldacchino et al. identified 200 follow-up studies of opioid exposures during pregnancy, but only 8 studies met inclusion criteria with 4 studies in infancy, 3 assessing preschool children, and 1 on school children[110,111]. All these were case-control studies conducted within urbanized, low socioeconomic communities, with mothers exposed to either heroin or methadone. Five studies had data usable for meta-analysis, with a total of 218 opioid-exposed and 205 non-exposed children. In all outcomes opioid-exposed children had lower scores as compared to controls[110].

10) Neurodevelopmental Consequences: Differences in neurodevelopment between children with and without exposure to prenatal opioids are related to the age at which they were assessed, with milder differences occurring at birth, greater differences during infancy and early childhood but widening gaps noted during school age and adolescence. Individuals with NAS at birth had impaired behavioral regulation, greater excitability and arousal, and poorer quality of their movements[112-121]. Among infants and toddlers, NAS was associated with impaired mental and language development as well as poorer neuromotor and psychomotor development before 24 months of age[122]. Because of the very limited roles for cognitive or executive functions in early childhood, studies performed in the younger age groups showed minimal differences in cognitive or executive functions with and without NAS[123,124] (e.g., every infant is likely to fail an algebra test). In contrast, the Bayley Scales of Infant Development revealed more prominent neurodevelopment deficits, with greater vulnerability among boys than in girls[125-127]. Assessment in later childhood revealed differences in IQ, motor performance[128-131], language performance[132], lower IQ scores, behavior and attention problems compared with unexposed children at 8.5 years of age[107,108]. Children exposed to methadone prenatally also had elevated levels of aggression, fear, and anxiety[91,130,133]. Even after controlling for their sociodemographic factors and birth mother's medical history, elevated symptoms of ADHD occurred in children who were exposed to prenatal opioids compared with children not exposed to opioids *in utero* [91,130,134].

A recent systematic review and meta-analysis of cohort studies of 1,455 children from birth to 18 years found that prenatal opioid exposures negatively impacted neurocognitive outcomes and physical/motor development from age 6 months onwards, and this association persisted until adolescence[135]. The study could not differentiate between the contributions of prenatal opioid exposure vs. opioid treatment for NAS after birth and recommended that all NAS children should receive long-term monitoring, with social, emotional and educational support or intervention[135]. The long-term effects of prenatal opioids on cognition tended to increase over time, even in those children who were adopted or placed in foster care, thus being exposed to minimal postnatal risk factors[107]. NAS children discharged home with their birth mother, despite a longer hospital stay, had a higher likelihood of being referred for early intervention services (81%) compared to those placed in foster care (66%)[136].

11) Executive Functions: Executive functions are thinking skills that help us with the information processing, reasoning, planning, problem-solving, for coping with stress, regulating our emotions and managing our lives. As a child progresses through school, the executive functions assume greater importance in their academic success, goal setting, and employability[137]. Children exposed to prenatal opioids have difficulties with information processing[138], poorer performance on a

vigilance task[139], lower overall executive functioning[105], significantly lower visual acuity[101], impaired visual-motor and perceptual performances, and fewer goal-directed eye movements[140-142]. Children with NAS were far more likely to have developmental delays and lower IQ[143], 2.3 times more likely to be hospitalized for neuropsychiatric disorders[144], 4.5 times more likely to be hospitalized for child abuse[144] and die during hospitalization[144], perform poorly on educational testing[145], and show cognitive disabilities requiring extra classroom therapies and services[146]. CDC compared 1815 children with NAS and 5441 children without NAS (age 3-8 years). Children with NAS were more likely referred for disability evaluation (19.3% vs. 13.7%), have a learning disability (15.6% vs. 11.7%) and require classroom therapies (15.3% vs. 11.4%). These differences remained significant even after controlling for maternal smoking, maternal education, birth weight, gestational age, and/or NICU admission[146]. Children with NAS had lower scores on standardized testing in grade 3; by grade 7, children with NAS were scoring lower than other children in grade 5 and showing progressively greater deficits[145]. The increasingly complex cognitive processing and executive functioning required within a competitive high school environment place these children with NAS at progressively greater disadvantage and much higher likelihood of adverse outcomes, thus widening the gap between those with and without NAS.

12) Neuropsychiatric outcomes: Although Uebel et al. (2015) had found that more children with NAS were hospitalized with neuropsychiatric disorders (adjustment, conduct, anxiety, emotional, or speech disorders), three recent studies have highlighted the very high prevalence and distribution of mental health conditions among individuals with prenatal opioids. Using a Medicaid database, Sherman et al. (2019) found that half of all children with NAS were diagnosed with mental disorder before age 5, compared with 30% of all other births. Children with NAS were more likely to have conduct disturbances (2.7-fold), hyperkinetic syndromes (2.6-fold), adjustment difficulties (2.5-fold), stress/anxiety disorders (1.5-fold), emotional problems (1.9-fold), childhood-onset psychoses (1.7-fold), intellectual disabilities (2.3-fold), specific developmental delays (1.7-fold)[147]. Mental health conditions were 1.6-fold more prevalent in children with a history of NAS than the opioid-exposed children without a history of NAS, and 1.4-fold higher among children with Medicaid vs. commercial health insurance (Table 2 from Conner et al., 2019)[148]. From a longitudinally followed youth cohort (17-22 years) with prenatal opioid exposures (± other drugs) who were adopted/fostered before 1 year of age, Nygaard et al. (2019) found **2- to 8-fold higher lifetime risk of mental disorders** compared to matched controls[149]. These risks mainly included

TABLE 2 Diagnoses of mental health conditions in children with and children without neonatal abstinence syndrome (NAS), by Medicaid or commercial insurance coverage

	Commercial insurance (N=1,405,712)				Medicaid[a] (N=270,772)			
	NAS (N=190)		No NAS (N=1,405,522)		NAS (N=1,046)		No NAS (N=269,726)	
Diagnosis (*ICD-9* code)	N	%	N	%	N	%	N	%
Any mental health condition/diagnosis	68	35.8	313,021	22.3	511	48.9	81,814	30.3
Specific delays in development (315)	48	25.3	115,785	8.2	327	31.3	49,591	18.4
Disturbance of conduct (312)	11	5.8	37,120	2.6	113	10.8	10,879	4.0
Hyperkinetic syndrome of childhood (314)	13	6.8	102,770	7.3	94	9.0	9,372	3.5
Adjustment reaction (309)	9	4.7	63,295	4.5	75	7.2	7,799	2.9
Acute reaction to stress (308)	2	1.1	6,995	.5	49	4.7	8,123	3.0
Neurotic disorders (300)	9	4.7	60,749	4.3	43	4.1	7,365	2.7
Special symptoms or syndromes (307)	11	5.8	58,585	4.2	41	3.9	9,672	3.6
Disturbance of emotion specific to childhood and adolescence (313)	2	1.1	23,686	1.7	39	3.7	5,350	2.0
Intellectual disabilities (317–319)	1	5	2,596	.2	37	3.5	4,074	1.5
Psychoses with origin specific to childhood (299)	8	4.2	26,860	1.9	32	3.1	4,752	1.8

[a] Source: Sherman et al., 2019 (2). Adapted by permission from American Psychiatric Association Publishing.

major depression, alcohol abuse, ADHD, and **aggressive behaviors** even after controlling for age, gender, and caregivers' education. These children not only engaged in sex at younger ages and had **more sexual partners** compared to controls, but also experienced **suicidality** (28.8%), **psychoses** (17.7%), or **antisocial personality disorder** (15.6%) more often than their peers[149].

Such bleak outcomes portend a future tsunami of neurocognitive and neuropsychiatric disorders among the children and youth with NAS. The Opioid Crisis has increased over the past 20 years; therefore, multiple generations of such children and youth have been affected. While we continue to argue about priorities and preferences, these children are growing up – and every day that passes without the medical monitoring or supportive services being offered to these children, it makes their problems more and more intractable, imposing on them poorer outcomes and greater societal disadvantages.

Urgent need for more scientific investigations of individuals with NAS

Despite the recent flurry of scientific publications on this topic, there are numerous unanswered questions about the epidemiology, risk factors, diagnoses, management, and responses to therapy in the children with NAS. Therefore, there is an urgent need for a court-appointed Science Panel with the imperative to document the long-term outcomes of children exposed to prenatal opioids, through multiple, well-designed, large studies that prospectively enroll adult women with OUD and ensure good retention rates, to longitudinally follow their children with NAS at least until 18 years of age. All these children will require detailed neurocognitive and neuropsychiatric testing, as well as functional monitoring. Such tests are not available during routine doctor visits or other healthcare settings. To be explicit, these needs exist well-above and beyond the routine pediatric care and/or schooling required for non-opioid exposed children. These needs are not currently covered by Medicaid, or any private health insurance or any kind of Special-Ed funding. To obtain such data and to ensure that appropriate therapies and social services are offered, these children require detailed medical monitoring and surveillance through a well-coordinated, standardized, multidisciplinary, and nationally implemented protocol as described below. The results of such monitoring and surveillance must be regularly evaluated by the court-appointed Science Panel, so that accumulating data and scientific insights can be applied to the ongoing care of these children. To inform members of the Science Panel, they must be given access to all scientific and medical studies, data, experiments, white papers, research forms, or other materials related to the synthetic opioids, regardless of whether such materials had ever been provided to the FDA or whether they were protected assert trade secret protection.

Protocol for monitoring/surveillance of children diagnosed with NAS

1) Biological variability is based on genetic and epigenetic mechanisms, or factors related to the prenatal opioid exposure that manifested NAS (specific drugs, dosage, period(s) of pregnancy affected, detox or treatment effects, exposures to smoking, alcohol, or other drugs), as well as the postnatal treatments for NAS. All these will influence the child's long-term neurodevelopmental consequences resulting from NAS. Individual differences occurring between humans are difficult to determine specifically, but a common medical monitoring program is absolutely essential for all NAS victims because they are all at high-risk for common detrimental outcomes, associated with 'hidden' or latent conditions and disorders that can be ameliorated through medical monitoring, scheduled assessments, surveillance procedures and appropriate therapies. The proposed monitoring is different from that normally recommended in the absence of opioid exposures and

there is immense clinical value in the early detection and diagnosis of long-term opioid effects. If our societal goal is to achieve the maximal developmental outcomes for all children, then uniform and robust program will be necessary. Although some children might ultimately benefit more than others, however, that can be attributed to a biological variability in response to therapy, other psychosocial factors, or presently unknown factors that require further scientific investigation.

2) Children with NAS are at higher risk for a variety of adverse outcomes as noted above. Therefore, they are worthy of a more structured and specialized program of monitoring and surveillance with scheduled extra assessments, for at least two reasons. First, their families/caregivers want to know if their child is healthy and growing and developing normally, and they want to know about the health or other problems likely to be encountered in the future. Special concerns often arise at childhood or social transition points, such as entering childcare or changing school levels, thus requiring careful guidance and advice. Second, most of their developmental problems can be ameliorated or prevented if detected early – identification of high-risk groups for targeted interventions can be both cost-effective and efficient. Multidisciplinary advice from Doyle et al. (2014)[150] was used to design the monitoring protocol as outlined below.

3) If these periodic diagnostic medical exams identify a particular deficit or disability, the child's caregivers must be provided access to the specific resources and treatment(s) that they will need to overcome the long-term impacts of NAS. Additionally, caring for a victim of NAS is difficult, associated with increased risks for repeated hospitalizations of the child. An educational program aimed at increasing the understanding of NAS in parents and other caregivers is recommended, including access (or referral) to resources for both the caregiver and the child.

4) Barriers for implementing standardized monitoring protocols must be anticipated and addressed. These may include providing funding for transportation to scheduled assessments or making the transport arrangements, providing token compensation to participants, facilitating access by offering home visits or assessments at a location convenient for the parent/caregiver, consideration for living situation, and other barriers.

5) Most of these assessments are required annually, unless specified otherwise. Certain specialist assessments may be required only once (e.g., cardiology evaluation to rule-out congenital heart disease), or to be determined by the results of the previous testing – more frequent assessments will be required for the NAS children with abnormal/atypical results.

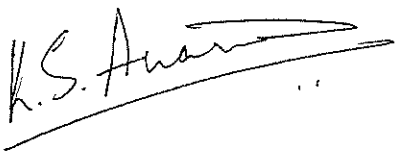
6) The data gained from these assessments must be deidentified, aggregated and securely stored in a state-level database, with query access available to researchers, practitioners, social or healthcare agencies, advocacy groups and others.

In conclusion, implementation of the studies referenced herein as well as the long-term care and treatment of these babies is essential to the resolution of the Opioid Crisis and its impact on our society. This report is based upon the information available at the time it was prepared. With the recent increase in NAS cases, the scientific understanding of NAS and the outcomes of NAS victims continues to evolve. And yet, much work remains to be done, which is the goal of implementing a long-term Court-appointed Science Panel – to study the results of the monitoring and surveillance and to recommend interventions as needs arise. With the Court's permission, I

would like to reserve the right to update this report in order to reflect the accumulating scientific and medical evidence as necessary.

I certify under penalty of perjury that the foregoing is true and correct.

Executed on December 8, 2019.



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References:

1. Terplan M. Beyond the Treatment Box: Perspectives on the Federal Response to Opioid Use, Pregnancy, and Neonatal Abstinence Syndrome. J Addict Med 2017;11:176-7.
2. Anand KJS, Willson DF, Berger J, et al. Tolerance and withdrawal from prolonged opioid use in critically ill children. Pediatrics 2010;125:e1208-25.
3. Anand KJS, Arnold JH. Opioid tolerance and dependence in infants and children. Crit Care Med 1994;22:334-42.
4. Suresh S, Anand KJS. Opioid tolerance in neonates: mechanisms, diagnosis, assessment, and management. Semin Perinatol 1998;22:425-33.
5. Suresh S, Anand KJS. Opioid tolerance in neonates: a state-of-the-art review. Paediatr Anaesth 2001;11:511-21.
6. Finnegan LP, Connaughton JF, Jr., Kron RE, Emich JP. Neonatal abstinence syndrome: assessment and management. Addict Dis 1975;2:141-58.
7. Finnegan LP, Kron RE, Connaughton JF, Emich JP. Assessment and treatment of abstinence in the infant of the drug-dependent mother. Int J Clin Pharmacol Biopharm 1975;12:19-32.
8. Lifshitz M, Gavrilov V, Galil A, Landau D. A four year survey of neonatal narcotic withdrawal: evaluation and treatment. Isr Med Assoc J 2001;3:17-20.
9. Zimmermann-Baer U, Notzli U, Rentsch K, Bucher HU. Finnegan neonatal abstinence scoring system: normal values for first 3 days and weeks 5-6 in non-addicted infants. Addiction 2010;105:524-8.
10. Kocherlakota P. Neonatal abstinence syndrome. Pediatrics 2014;134:e547-61.
11. Tolia VN, Patrick SW, Bennett MM, et al. Increasing incidence of the neonatal abstinence syndrome in U.S. neonatal ICUs. N Engl J Med 2015;372:2118-26.
12. Maguire D, Cline GJ, Parnell L, Tai CY. Validation of the Finnegan neonatal abstinence syndrome tool-short form. Adv Neonatal Care 2013;13:430-7.
13. Gomez Pomar E, Finnegan LP, Devlin L, et al. Simplification of the Finnegan Neonatal Abstinence Scoring System: retrospective study of two institutions in the USA. BMJ Open 2017;7:e016176.
14. Lipsitz PJ. A proposed narcotic withdrawal score for use with newborn infants. A pragmatic evaluation of its efficacy. Clin Pediatr (Phila) 1975;14:592-4.
15. Rivers RP. Neonatal opiate withdrawal. Arch Dis Child 1986;61:1236-9.
16. Green M, Suffet F. The Neonatal Narcotic Withdrawal Index: a device for the improvement of care in the abstinence syndrome. Am J Drug Alcohol Abuse 1981;8:203-13.
17. Yam P, Lok L, Eastwood J, et al. Validation of hospital discharge coding for neonatal abstinence syndrome. Acta Paediatr 2019;108:1786-92.
18. Maalouf FI, Cooper WO, Stratton SM, et al. Positive Predictive Value of Administrative Data for Neonatal Abstinence Syndrome. Pediatrics 2019;143.
19. Timpson W, Killoran C, Maranda L, Picarillo A, Bloch-Salisbury E. A Quality Improvement Initiative to Increase Scoring Consistency and Accuracy of the Finnegan Tool: Challenges in Obtaining Reliable Assessments of Drug Withdrawal in Neonatal Abstinence Syndrome. Adv Neonatal Care 2018;18:70-8.

20. Nechanska B, Mravcik V, Skurtveit S, et al. Neonatal outcomes after fetal exposure to methadone and buprenorphine: national registry studies from the Czech Republic and Norway. Addiction 2018;113:1286-94.
21. Haight SC, Ko JY, Tong VT, Bohm MK, Callaghan WM. Opioid Use Disorder Documented at Delivery Hospitalization - United States, 1999-2014. MMWR Morb Mortal Wkly Rep 2018;67:845-9.
22. Martin JA, Hamilton BE, Osterman MJ, Driscoll AK, Mathews TJ. Births: Final Data for 2015. Natl Vital Stat Rep 2017;66:1.
23. Martin JA, Hamilton BE, Osterman MJK, Driscoll AK, Drake P. Births: Final Data for 2016. Natl Vital Stat Rep 2018;67:1-55.
24. Hamilton BE, Martin JA, Osterman MJ, Driscoll AK, Rossen LM. Births: Provisional Data for 2017. Washington, DC: Centers for Disease Control & Prevention, U.S. Department of Health and Human Services; 2018.
25. Patrick SW, Schumacher RE, Benneyworth BD, Krans EE, McAllister JM, Davis MM. Neonatal abstinence syndrome and associated health care expenditures: United States, 2000-2009. JAMA 2012;307:1934-40.
26. Atwell KA, Weiss HB, Gibson C, Miller R, Corden TE. Neonatal Abstinence Syndrome and Maternal Substance Use in Wisconsin, 2009-2014. WMJ 2016;115:287-94.
27. Ko JY, Patrick SW, Tong VT, Patel R, Lind JN, Barfield WD. Incidence of Neonatal Abstinence Syndrome - 28 States, 1999-2013. MMWR Morb Mortal Wkly Rep 2016;65:799-802.
28. Ko JY, Wolicki S, Barfield WD, et al. CDC Grand Rounds: Public Health Strategies to Prevent Neonatal Abstinence Syndrome. MMWR Morb Mortal Wkly Rep 2017;66:242-5.
29. Reddy UM, Davis JM, Ren Z, Greene MF, Opioid Use in Pregnancy NAS, Childhood Outcomes Workshop Invited S. Opioid Use in Pregnancy, Neonatal Abstinence Syndrome, and Childhood Outcomes: Executive Summary of a Joint Workshop by the Eunice Kennedy Shriver National Institute of Child Health and Human Development, American College of Obstetricians and Gynecologists, American Academy of Pediatrics, Society for Maternal-Fetal Medicine, Centers for Disease Control and Prevention, and the March of Dimes Foundation. Obstet Gynecol 2017;130:10-28.
30. Kraft WK, Stover MW, Davis JM. Neonatal abstinence syndrome: Pharmacologic strategies for the mother and infant. Semin Perinatol 2016;40:203-12.
31. Patrick SW, Davis MM, Lehmann CU, Cooper WO. Increasing incidence and geographic distribution of neonatal abstinence syndrome: United States 2009 to 2012. J Perinatol 2015;35:650-5.
32. Patrick SW, Dudley J, Martin PR, et al. Prescription opioid epidemic and infant outcomes. Pediatrics 2015;135:842-50.
33. Brandt L, Finnegan LP. Neonatal abstinence syndrome: where are we, and where do we go from here? Curr Opin Psychiatry 2017;30:268-74.
34. Jansson LM, Velez M, Harrow C. The opioid-exposed newborn: assessment and pharmacologic management. J Opioid Manag 2009;5:47-55.
35. McQueen KA, Murphy-Oikonen J, Desaulniers L. Maternal Substance Use and Neonatal Abstinence Syndrome: A Descriptive Study. Matern Child Health J 2015;19:1756-65.
36. Hytinantti T, Kahila H, Renlund M, Jarvenpaa AL, Halmesmaki E, Kivitie-Kallio S. Neonatal outcome of 58 infants exposed to maternal buprenorphine in utero. Acta Paediatr 2008;97:1040-4.
37. Lind JN, Petersen EE, Lederer PA, et al. Infant and maternal characteristics in neonatal abstinence syndrome--selected hospitals in Florida, 2010-2011. MMWR Morb Mortal Wkly Rep 2015;64:213-6.
38. Okoroh EM, Gee RE, Jiang B, McNeil MB, Hardy-Decuir BA, Zapata AL. Neonatal Abstinence Syndrome: Trend and Expenditure in Louisiana Medicaid, 2003-2013. Matern Child Health J 2017;21:1479-87.
39. Wolff K, Perez-Montejano R. Opioid neonatal abstinence syndrome: controversies and implications for practice. Curr Drug Abuse Rev 2014;7:44-58.
40. Broussard CS, Rasmussen SA, Reefhuis J, et al. Maternal treatment with opioid analgesics and risk for birth defects. Am J Obstet Gynecol 2011;204:314 e1-11.
41. Yazdy MM, Mitchell AA, Tinker SC, Parker SE, Werler MM. Periconceptional use of opioids and the risk of neural tube defects. Obstet Gynecol 2013;122:838-44.
42. Dawson AL, Razzaghi H, Arth A, et al. Maternal exposures in the National Birth Defects Prevention Study: Time trends of selected exposures. Birth Defects Res A Clin Mol Teratol 2015;103:703-12.
43. McCarthy M. Opioids are commonly prescribed to women of reproductive age despite birth defect risk, US CDC study shows. BMJ 2015;350:h456.
44. Interrante JD, Ailes EC, Lind JN, et al. Risk comparison for prenatal use of analgesics and selected birth defects, National Birth Defects Prevention Study 1997-2011. Ann Epidemiol 2017;27:645-53 e2.
45. Lind JN, Interrante JD, Ailes EC, et al. Maternal Use of Opioids During Pregnancy and Congenital Malformations: A Systematic Review. Pediatrics 2017;139.

46. Ballard JL. Treatment of neonatal abstinence syndrome with breast milk containing methadone. J Perinat Neonatal Nurs 2002;15:76-85.
47. Bell SG. Buprenorphine: a newer drug for treating neonatal abstinence syndrome. Neonatal Netw 2012;31:178-83.
48. Kraft WK, van den Anker JN. Pharmacologic management of the opioid neonatal abstinence syndrome. Pediatr Clin North Am 2012;59:1147-65.
49. Bagley SM, Wachman EM, Holland E, Brogly SB. Review of the assessment and management of neonatal abstinence syndrome. Addict Sci Clin Pract 2014;9:19.
50. Patrick SW, Kaplan HC, Passarella M, Davis MM, Lorch SA. Variation in treatment of neonatal abstinence syndrome in US children's hospitals, 2004-2011. J Perinatol 2014;34:867-72.
51. McPherson C. Pharmacotherapy for Neonatal Abstinence Syndrome: Choosing the Right Opioid or No Opioid at All. Neonatal Netw 2016;35:314-20.
52. Grossman MR, Berkwitt AK, Osborn RR, et al. An Initiative to Improve the Quality of Care of Infants With Neonatal Abstinence Syndrome. Pediatrics 2017;139.
53. Kraft WK, Adeniyi-Jones SC, Chervoneva I, et al. Buprenorphine for the Treatment of the Neonatal Abstinence Syndrome. N Engl J Med 2017;376:2341-8.
54. Kraft WK, Adeniyi-Jones SC, Ehrlich ME. Buprenorphine for the Neonatal Abstinence Syndrome. N Engl J Med 2017;377:997-8.
55. Pryor JR, Maalouf FI, Krans EE, Schumacher RE, Cooper WO, Patrick SW. The opioid epidemic and neonatal abstinence syndrome in the USA: a review of the continuum of care. Arch Dis Child Fetal Neonatal Ed 2017;102:F183-F7.
56. Gadomski A, Riley M, Ramiza K, et al. Treating Neonatal Abstinence Syndrome in a Rural Hospital: Lessons Learned. Acad Pediatr 2018.
57. Jimenez-Gonzalez A, Garcia-Concejo A, Leon-Lobera F, Rodriguez RE. Morphine delays neural stem cells differentiation by facilitating Nestin overexpression. Biochim Biophys Acta 2018;1862:474-84.
58. Madden JJ, Falek A, Shafer DA, Glick JH. Effects of opiates and demographic factors on DNA repair synthesis in human leukocytes. Proc Natl Acad Sci U S A 1979;76:5769-73.
59. McLaughlin P, Mactier H, Gillis C, et al. Increased DNA Methylation of ABCB1, CYP2D6, and OPRM1 Genes in Newborn Infants of Methadone-Maintained Opioid-Dependent Mothers. J Pediatr 2017;190:180-4 e1.
60. Drobnis EZ, Nangia AK. Pain Medications and Male Reproduction. Adv Exp Med Biol 2017;1034:39-57.
61. Abo-Elnazar S, Moaaz M, Ghoneim H, Molokhia T, El-Korany W. Th17/Treg imbalance in opioids and cannabinoids addiction: relationship to NF-kappaB activation in CD4+ T cells. Egypt J Immunol 2014;21:33-47.
62. Feng YM, Jia YF, Su LY, et al. Decreased mitochondrial DNA copy number in the hippocampus and peripheral blood during opiate addiction is mediated by autophagy and can be salvaged by melatonin. Autophagy 2013;9:1395-406.
63. Perez-Alvarez S, Iglesias-Guimarais V, Solesio ME, et al. Methadone induces CAD degradation and AIF-mediated necrotic-like cell death in neuroblastoma cells. Pharmacol Res 2011;63:352-60.
64. Hu S, Sheng WS, Lokensgard JR, Peterson PK. Morphine induces apoptosis of human microglia and neurons. Neuropharmacology 2002;42:829-36.
65. Zagon IS, Verderame MF, Allen SS, McLaughlin PJ. Cloning, sequencing, chromosomal location, and function of cDNAs encoding an opioid growth factor receptor (OGFr) in humans. Brain Res 2000;856:75-83.
66. Zagon IS, Wu Y, McLaughlin PJ. Opioid growth factor and organ development in rat and human embryos. Brain Res 1999;839:313-22.
67. Madden JJ, Falek A. The use of nonneuronal cells as an in vitro model system for studying the genetic component of cellular response to opiates and other drugs of abuse. J Addict Dis 1991;10:229-38.
68. Falek A, Donahoe RM, Madden JJ, Shafer DA. Opiates as immunosuppressive and genotoxic agents. Adv Exp Med Biol 1991;288:189-201.
69. Shafer DA, Falek A, Donahoe RM, Madden JJ. Biogenetic effects of opiates. Int J Addict 1990;25:1-18.
70. Falek A, Madden JJ, Shafer DA, Donahoe RM. Individual differences in opiate-induced alterations at the cytogenetic, DNA repair, and immunologic levels: opportunity for genetic assessment. NIDA Res Monogr 1986;66:11-24.
71. Shafer DA, Falek A, Madden JJ, et al. Parallel increases in sister-chromatid exchanges at base level and with UV treatment in human opiate users. Mutat Res 1983;109:73-82.
72. McCarthy JJ, Leamon MH, Finnegan LP, Fassbender C. Opioid dependence and pregnancy: minimizing stress on the fetal brain. Am J Obstet Gynecol 2017;216:226-31.
73. Wachman EM, Hayes MJ, Lester BM, et al. Epigenetic variation in the mu-opioid receptor gene in infants with neonatal abstinence syndrome. J Pediatr 2014;165:472-8.
74. Hurd YL, O'Brien CP. Molecular Genetics and New Medication Strategies for Opioid Addiction. Am J Psychiatry 2018:appiajp201818030352.

75. Goldberg LR, Gould TJ. Multigenerational and transgenerational effects of paternal exposure to drugs of abuse on behavioral and neural function. Eur J Neurosci 2018.
76. Crist RC, Reiner BC, Berrettini WH. A review of opioid addiction genetics. Curr Opin Psychol 2018;27:31-5.
77. Marie-Claire C, Jourdaine C, Lepine JP, Bellivier F, Bloch V, Vorspan F. Pharmacoepigenomics of opiates and methadone maintenance treatment: current data and perspectives. Pharmacogenomics 2017;18:1359-72.
78. Marie-Claire C, Crettol S, Cagnard N, et al. Variability of response to methadone: genome-wide DNA methylation analysis in two independent cohorts. Epigenomics 2016;8:181-95.
79. Andersen AM, Dogan MV, Beach SR, Philibert RA. Current and Future Prospects for Epigenetic Biomarkers of Substance Use Disorders. Genes (Basel) 2015;6:991-1022.
80. Nielsen DA, Utrankar A, Reyes JA, Simons DD, Kosten TR. Epigenetics of drug abuse: predisposition or response. Pharmacogenomics 2012;13:1149-60.
81. Oei JL, Xu HX, Abdel-Latif ME, et al. Dopamine D2 receptor gene polymorphisms in newborn infants of drug-using women. Arch Dis Child Fetal Neonatal Ed 2012;97:F193-8.
82. Anand KJS, Campbell-Yeo M. Consequences of prenatal opioid use for newborns. Acta Paediatr 2015;104:1066-9.
83. Svensson A-L, Bucht N, Hallberg M, Nyberg F. Reversal of opiate induced apoptosis by human recombinant growth hormone in murine foetus primary hippocampal neuronal cell cultures. PNAS 2008;105:7304-8.
84. Durmeyer X, Vutskits L, Anand KJS, Rimensberger PC. Use of analgesic and sedative drugs in the NICU: integrating clinical trials and laboratory data. Pediatr Res 2010;67:117-27.
85. Nassogne M-C, Evrard P, Courtoy PJ. Selective neuronal toxicity of Cocaine in empryonic mouse brain co-cultures. PNAS 1995;92:11029-33.
86. Clowry G, Molnar Z, Rakic P. Renewed focus on the developing human neocortex. J Anat 2010;217:276-88.
87. Yuan Q, Rubic M, Seah J, et al. Do maternal opioids reduce neonatal regional brain volumes? A pilot study. J Perinatol 2014;34:909-13.
88. Nygaard E, Slinning K, Moe V, Due-Tonnessen P, Fjell A, Walhovd KB. Neuroanatomical characteristics of youths with prenatal opioid and poly-drug exposure. Neurotoxicol Teratol 2018;68:13-26.
89. van den Bosch GE, White T, El Marroun H, et al. Prematurity, Opioid Exposure and Neonatal Pain: Do They Affect the Developing Brain? Neonatology 2015;108:8-15.
90. Yazdy MM, Desai RJ, Brogly SB. Prescription opioids in pregnancy and birth outcomes a review of the literature. J Pediatric Genetics 2015;4:56-70.
91. Ornoy A, Michailevskaya V, Lukashov I, Bar-Hamburger R, Harel S. The developmental outcome of children born to heroin-dependent mothers, raised at home or adopted. Child Abuse Negl 1996;20:385-96.
92. Bier JB, Finger AS, Bier BA, Johnson TA, Coyle MG. Growth and developmental outcome of infants with in-utero exposure to methadone vs buprenorphine. J Perinatol 2015;35:656-9.
93. Brogly SB, Saia KA, Walley AY, Du HM, Sebastiani P. Prenatal buprenorphine versus methadone exposure and neonatal outcomes: systematic review and meta-analysis. Am J Epidemiol 2014;180:673-86.
94. Garrison L, Leeman L, Savich RD, Gutierrez H, Rayburn WF, Bakhireva LN. Fetal Growth Outcomes in a Cohort of Polydrug- and Opioid-Dependent Patients. J Reprod Med 2016;61:311-9.
95. Jones HE, Dengler E, Garrison A, et al. Neonatal outcomes and their relationship to maternal buprenorphine dose during pregnancy. Drug Alcohol Depend 2014;134:414-7.
96. Kelty E, Hulse G. A Retrospective Cohort Study of Birth Outcomes in Neonates Exposed to Naltrexone in Utero: A Comparison with Methadone-, Buprenorphine- and Non-opioid-Exposed Neonates. Drugs 2017;77:1211-9.
97. Visconti KC, Hennessy KC, Towers CV, Howard BC. Chronic opiate use in pregnancy and newborn head circumference. Am J Perinatol 2015;32:27-32.
98. Wiegand SL, Stringer EM, Stuebe AM, Jones H, Seashore C, Thorp J. Buprenorphine and naloxone compared with methadone treatment in pregnancy. Obstet Gynecol 2015;125:363-8.
99. Zedler BK, Mann AL, Kim MM, et al. Buprenorphine compared with methadone to treat pregnant women with opioid use disorder: a systematic review and meta-analysis of safety in the mother, fetus and child. Addiction 2016;111:2115-28.
100. Mactier H, Shipton D, Dryden C, Tappin DM. Reduced fetal growth in methadone-maintained pregnancies is not fully explained by smoking or socio-economic deprivation. Addiction 2014;109:482-8.
101. Walhovd KB, Bjornebekk A, Haabrekke K, et al. Child neuroanatomical, neurocognitive, and visual acuity outcomes with maternal opioid and polysubstance detoxification. Pediatr Neurol 2015;52:326-32 e1-3.
102. Sarfi M, Smith L, Waal H, Sundet JM. Risks and realities: dyadic interaction between 6-month-old infants and their mothers in opioid maintenance treatment. Infant Behav Dev 2011;34:578-89.
103. McGlone L, Mactier H. Infants of opioid-dependent mothers: neurodevelopment at six months. Early Hum Dev 2015;91:19-21.

104. Melinder A, Konijnenberg C, Sarfi M. Deviant smooth pursuit in preschool children exposed prenatally to methadone or buprenorphine and tobacco affects integrative visuomotor capabilities. Addiction 2013;108:2175-82.
105. Konijnenberg C, Sarfi M, Melinder A. Mother-child interaction and cognitive development in children prenatally exposed to methadone or buprenorphine. Early Hum Dev 2016;101:91-7.
106. Mactier H. Neonatal and longer term management following substance misuse in pregnancy. Early Hum Dev 2013;89:887-92.
107. Nygaard E, Moe V, Slinning K, Walhovd KB. Longitudinal cognitive development of children born to mothers with opioid and polysubstance use. Pediatr Res 2015;78:330-5.
108. Nygaard E, Slinning K, Moe V, Walhovd KB. Behavior and Attention Problems in Eight-Year-Old Children with Prenatal Opiate and Poly-Substance Exposure: A Longitudinal Study. PLoS One 2016;11:e0158054.
109. Nygaard E, Slinning K, Moe V, Walhovd KB. Cognitive function of youths born to mothers with opioid and poly-substance abuse problems during pregnancy. Child Neuropsychol 2017;23:159-87.
110. Baldacchino A, Arbuckle K, Petrie DJ, McCowan C. Neurobehavioral consequences of chronic intrauterine opioid exposure in infants and preschool children: a systematic review and meta-analysis. BMC Psychiatry 2014;14:104.
111. Baldacchino A, Arbuckle K, Petrie DJ, McCowan C. Erratum: neurobehavioral consequences of chronic intrauterine opioid exposure in infants and preschool children: a systematic review and meta-analysis. BMC Psychiatry 2015;15:134.
112. Bernstein V, Jeremy RJ, Hans SL, Marcus J. A longitudinal study of offspring born to methadone-maintained women. II. Dyadic interaction and infant behavior at 4 months. Am J Drug Alcohol Abuse 1984;10:161-93.
113. Marcus J, Hans SL, Jeremy RJ. A longitudinal study of offspring born to methadone-maintained women. III. Effects of multiple risk factors on development at 4, 8, and 12 months. Am J Drug Alcohol Abuse 1984;10:195-207.
114. Jeremy RJ, Hans SL. Behavior of neonates exposed in utero to methadone as assessed on the Brazelton scale. Infant Behav Dev 1985;8:323–36.
115. Johnson HL, Rosen TS. Prenatal methadone exposure: effects on behavior in early infancy. Pediatr Pharmacol (New York) 1982;2:113-20.
116. Lifschltz MH, Wilson GS. Patterns of growth and development in narcotic-exposed children. NIDA Res Monogr 1991;114:323-39.
117. Rosen TS, Johnson HL. Children of methadone-maintained mothers: follow-up to 18 months of age. J Pediatr 1982;101:192-6.
118. Wilson GS, Desmond MM, Wait RB. Follow-up of methadone-treated and untreated narcotic-dependent women and their infants: health, developmental, and social implications. J Pediatr 1981;98:716-22.
119. Hans SL, Marcus J. Motoric and attentional behavior in infants of methadone-maintained women. NIDA Res Monogr 1983;43:287-93.
120. Jones HE, O'Grady KE, Johnson RE, Velez M, Jansson LM. Infant neurobehavior following prenatal exposure to methadone or buprenorphine: results from the neonatal intensive care unit network neurobehavioral scale. Subst Use Misuse 2010;45:2244-57.
121. Heller NA, Logan BA, Morrison DG, Paul JA, Brown MS, Hayes MJ. Neonatal abstinence syndrome: Neurobehavior at 6 weeks of age in infants with or without pharmacological treatment for withdrawal. Dev Psychobiol 2017;59:574-82.
122. Conradt E, Flannery T, Aschner JL, et al. Prenatal Opioid Exposure: Neurodevelopmental Consequences and Future Research Priorities. Pediatrics 2019;144.
123. Hans SL, Jeremy RJ. Postneonatal mental and motor development of infants exposed in utero to opioid drugs. Infant Mental Health J 2001;22:300-15.
124. Levine TA, Woodward LJ. Early inhibitory control and working memory abilities of children prenatally exposed to methadone. Early Hum Dev 2018;116:68-75.
125. Merhar SL, McAllister JM, Wedig-Stevie KE, Klein AC, Meinzen-Derr J, Poindexter BB. Retrospective review of neurodevelopmental outcomes in infants treated for neonatal abstinence syndrome. J Perinatol 2018;38:587-92.
126. Moe V, Slinning K. Prenatal drug exposure and the conceptualization of long-term effects. Scand J Psychol 2002;43:41-7.
127. Moe V, Slinning K. Children prenatally exposed to substances: gender-related differences in outcome from infancy to 3 years of age. Infant Ment Health J 2001;22:334-50.
128. van Baar AL, Soepatmi S, Gunning WB, Akkerhuis GW. Development after prenatal exposure to cocaine, heroin and methadone. Acta Paediatr Suppl 1994;404:40-6.
129. Davis DD, Templer DI. Neurobehavioral functioning in children exposed to narcotics in utero. Addict Behav 1988;13:275-83.
130. Ornoy A, Segal J, Bar-Hamburger R, Greenbaum C. Developmental outcome of school-age children born to mothers with heroin dependency: importance of environmental factors. Dev Med Child Neurol 2001;43:668-75.

131. Wilson GS, McCreary R, Kean J, Baxter JC. The development of preschool children of heroin-addicted mothers: a controlled study. Pediatrics 1979;63:135-41.
132. Hunt RW, Tzioumi D, Collins E, Jeffery HE. Adverse neurodevelopmental outcome of infants exposed to opiate in-utero. Early Hum Dev 2008;84:29-35.
133. de Cubas MM, Field T. Children of methadone-dependent women: developmental outcomes. Am J Orthopsychiatry 1993;63:266-76.
134. Sandtorv LB, Fevang SKE, Nilsen SA, et al. Symptoms Associated With Attention Deficit/Hyperactivity Disorder and Autism Spectrum Disorders in School-Aged Children Prenatally Exposed to Substances. Subst Abuse 2018;12:1178221818765773.
135. Yeoh SL, Eastwood J, Wright IM, et al. Cognitive and Motor Outcomes of Children With Prenatal Opioid Exposure: A Systematic Review and Meta-analysis. JAMA Netw Open 2019;2:e197025.
136. Peacock-Chambers E, Leyenaar JK, Foss S, et al. Early Intervention Referral and Enrollment Among Infants with Neonatal Abstinence Syndrome. J Dev Behav Pediatr 2019;40:441-50.
137. Blair C. Educating executive function. Wiley Interdiscip Rev Cogn Sci 2017;8.
138. Guo X, Spencer JW, Suess PE, Hickey JE, Better WE, Herning RI. Cognitive brain potential alterations in boys exposed to opiates: in utero and lifestyle comparisons. Addict Behav 1994;19:429-41.
139. Hickey JE, Suess PE, Newlin DB, Spurgeon L, Porges SW. Vagal tone regulation during sustained attention in boys exposed to opiates in utero. Addict Behav 1995;20:43-59.
140. Konijnenberg C, Melinder A. Neurodevelopmental investigation of the mirror neurone system in children of women receiving opioid maintenance therapy during pregnancy. Addiction 2013;108:154-60.
141. Moe V. Foster-placed and adopted children exposed in utero to opiates and other substances: prediction and outcome at four and a half years. J Dev Behav Pediatr 2002;23:330-9.
142. Walhovd KB, Bjørnebekk A, Haabrekke K, al. e. Child neuroanatomical, neurocognitive, and visual acuity outcomes with maternal opioid and polysubstance detoxification. Pediatr Neurol 2015;52:326-32.
143. Bauman PS, Levine SA. The development of children of drug addicts. Int J Addict 1986;21:849-63.
144. Uebel H, Wright IM, Burns L, et al. Reasons for Rehospitalization in Children Who Had Neonatal Abstinence Syndrome. Pediatrics 2015;136:e811-20.
145. Oei JL, Melhuish E, Uebel H, et al. Neonatal Abstinence Syndrome and High School Performance. Pediatrics 2017;139.
146. Fill MA, Miller AM, Wilkinson RH, et al. Educational Disabilities Among Children Born With Neonatal Abstinence Syndrome. Pediatrics 2018;142:pii: e20180562.
147. Sherman LJ, Ali MM, Mutter R, Larson J. Mental Disorders Among Children Born With Neonatal Abstinence Syndrome. Psychiatr Serv 2019;70:151.
148. Conner KL, Meadows AL, Delcher C, Talbert JC. Neonatal Abstinence Syndrome and Childhood Mental Health Conditions, 2009–2015: Commercial Versus Medicaid Populations. Psychiatric Services 2019;(Advance Publication).
149. Nygaard E, Slinning K, Moe V, Fjell A, Walhovd KB. Mental health in youth prenatally exposed to opioids and poly-drugs and raised in permanent foster/adoptive homes: A prospective longitudinal study. Early Hum Dev 2019;140:104910.
150. Doyle LW, Anderson PJ, Battin M, et al. Long term follow up of high risk children: who, why and how? BMC Pediatr 2014;14:279.